

# CASE REPORT

## ◀ Pulmonary Endarteritis Obliterans With Cor Pulmonale Simulating Congenital Heart Disease

### Pulmonary Endarteritis Obliterans With Cor Pulmonale Simulating Congenital Heart Disease

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PRIMARY pulmonary vascular endarteritis obliterans in children is exceedingly rare. Necrotizing pulmonary arteritis or so-called periarteritis nodosa occurring with congenital heart disease (Eisenmenger type) has been reported by Old and Russell<sup>1</sup> and Kipkie and Johnson.<sup>3</sup> Both cases occurred in 11-year-old boys. Brill and Krygier<sup>1</sup> reviewed reports of 20 cases of primary pulmonary vascular arteriosclerosis and noted that four of the patients were children 11 to 15 years of age. In these cases intimal proliferation was noted in the pulmonary arterioles, and there was pronounced narrowing or complete occlusion of the lumens, while in the small arterioles were thrombi of various ages and recanalization. In many of the cases complete obliteration and hyalinization of the capillary vessels was noted. There were no pathologic changes in the lungs, but enlargement of the right side of the heart was noted. Brill and Krygier concluded that the condition was the result of either infectious or degenerative change.

Harrison<sup>2</sup> experimentally was able to demonstrate lesions in the pulmonary artery of rabbits given intravenous injections of finely fragmented fibrin clot similar to that described in pulmonary vascular arteriosclerosis as a result of pulmonary emboli. Fibroelastic intimal thickening of the vessels, morphologically indistinguishable from that of spontaneous arteriosclerosis, was observed in the healed lesions. Harrison concluded that in some of the cases reported as primary pulmonary arteriosclerosis because of this histological appearance, the structure might actually have been the result of embolism.

The case to be reported is unique in that the vascular lesions were restricted to the pulmonary arteries. Rheumatic fever as an etiological factor could not be excluded. Shortness of breath, cyanosis, peripheral edema, tachycardia, cough, a harsh systolic murmur in the anterior axillary line, and a palpable systolic thrill suggested the presence of congenital heart disease. At autopsy, pronounced hypertrophy of the right ventricle was noted but there were no malformations.

#### CASE REPORT

A nine-year-old Mexican female child was admitted to the San Bernardino County Hospital May 29, 1950, with complaints of cough of increasing severity for one week, shortness of breath and fever for one day. There was some nausea and vomiting, and also some pain in the left ear. The patient had been in fairly good health until the present illness. The parents noted that the child had fever and that the breathing was rapid the day before admittance.

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The patient appeared to be chronically ill; she was slender and emaciated, the body weight approximately 35 pounds. The temperature was 101.6°, the pulse rate 148 and respiration 40 per minute. There was no discharge from the ears and the ear drums were clear. The pupils were regular, equal and reacted to light and accommodation. The teeth were in poor condition and many were missing. No abnormality was noted in the pharynx. There was an old skin scar on the left side of the neck, and the carotid artery on that side was large and pulsating. Lymph nodes in the neck were not enlarged. The chest was clear to auscultation. The abdomen was scaphoid. No tenderness was noted and there were no palpable masses. The heart rate was rapid and a grade II mitral murmur, heard best at the apex, was noted. The fingernails were curved, but there was no clubbing or cyanosis.

The clinical impression was that the patient had a mild upper respiratory tract infection, congenital or acquired heart disease, possibly rheumatic, avitaminosis, and, possibly, carotid aneurysm.

Erythrocytes numbered 4,900,000 per cu. mm., and the hemoglobin value was 75 per cent (12.9 gm. per 100 cc.). Leukocytes numbered 9,300—79 per cent neutrophils, 19 per cent lymphocytes, and 2 per cent monocytes. Results of urinalysis were within normal limits. In an electrocardiogram, sinus tachycardia and right axis deviation, considered abnormal, were noted. The nonprotein nitrogen content of the blood was 36 mg. per 100 cc.

In roentgen examination of the chest, the lung fields were observed to be clear and the cardiovascular shadow within normal limits. The primary pulmonary vessels at the hila were distended and engorged.

The child had been delivered by cesarean section at eight months in the San Bernardino County Hospital. (The mother had had chronic nephritis associated with toxemia of pregnancy.) The infant weighed 4 pounds 11.5 ounces at birth. There was a swelling on the left side of the neck beneath the mandible and over the left scapula, and on the back of the neck. A week after birth the mass was aspirated and a diagnosis of cystic hygroma was made. In January 1943, the child was a patient at the Children's Hospital in Los Angeles because of suppurative otitis media of the left ear and an abscess below the left ear. Under sulfonamide therapy the ear gradually dried and the abscess became smaller. Subsequently, the hygromic mass was opened and drained and the left carotid artery was ligated. In 1944 the cystic mass was removed and a pathological diagnosis of cystic hygroma was made. The child apparently did well until the present illness. There was no note of a murmur over the heart in the records of the many examinations of the patient.

The day after admittance to hospital, the temperature rose to 103° F. On the third day it was normal and remained normal. The morning after admittance rales heard in the right mid-lung field were considered probably caused by pneumonia. The suspicion of aneurysm of the left carotid artery was not substantiated, and the prominence of the pulsation of the artery was considered due to the absence of the sternocleidomastoid muscle, which had

been removed. Reaction to a tuberculin test was interpreted as positive, which raised the question of tuberculous pneumonia. After 18 days in the hospital the child was discharged with a diagnosis of primary juvenile tuberculosis. The parents were advised to keep her in bed at home.

The child was readmitted July 27, 1950, because of generalized edema associated with cough. A week before, the left side of the face and then the left leg became swollen. The child had been in bed, propped with pillows because of respiratory embarrassment. There was no pain around the heart, but there had been pain in the left leg for several weeks. The appetite had been poor.

Upon examination the patient was noted to be poorly nourished, very orthopneic and dyspneic. The abdomen was distended and the left side of the face was swollen. Dullness was noted in the apex of the left lung anteriorly. The remainder of the chest was hyperresonant. No rales were heard. The heart seemed to be enlarged to the anterior axillary line. There was a blowing, harsh systolic murmur at the apex, not transmitted, and a thrill was felt over the same area. The liver was palpable down to the umbilicus. There was pitting edema (+ +) of the legs up to the knees.

Erythrocytes numbered 5,850,000 per cu. mm. and the hemoglobin content was 15.6 gm. per 100 cc. Leukocytes numbered 4,850, with the cell differential within normal limits.

In roentgen examination of the chest (Figure 1) on August 2, 1950, generalized increase in the lung markings, suggesting congestion, was noted. The cardiac shadow was enlarged. In an electrocardiogram taken August 1, there was evidence of sinus tachycardia and right axis deviation.

The patient was given meralluride and digitoxin, ascorbic acid and ammonium chloride. On August 3 the erythrocyte sedimentation rate was 19 mm. in one hour. The child had fever and remained dyspneic. The pulse rate dropped to about 110 per minute. The apex beat was noticed in the third interspace. There was a harsh, blowing systolic murmur, and a diastolic and presystolic component at the apex. The murmur became shrill at the midaxillary line. The lungs, however, were clear.

On August 19 salicylates were given but caused vomiting. Digitoxin and acetylsalicylic acid also had to be discontinued. On August 23, the child became listless and apathetic, and gavage feedings were started. Two days later the heart murmur, harsh and high-pitched, was interpreted as being systolic at the apex, and it was also heard over the pulmonic area. Cyanosis was noted for the first time.

No conclusion could be reached as to whether the abnormalities in the heart were of congenital or rheumatic origin. On August 29 the child became afebrile. Another physician who examined the patient on September 7 made the following report: "Nine years of age, the patient had the body development of a child of five. She was definitely cyanotic. There was no clubbing of the fingers, lobes of the ears or nose. No increase in the number of capillaries in the conjunctiva or eye grounds was noted. The veins of the sublingual and pharyngeal areas were not abnormally engorged. Pronounced venous pulsation in the left side of the neck was dicrotic and not caused by an underlying carotid aneurysm. When the patient lay down, the veins on the right side of the neck filled. The lungs were clear throughout. The heart was definitely enlarged; the point of maximum impulse was in the fourth interspace at the anterior axillary line. In the third left interspace, just at the anterior axillary line, a very definite systolic thrill could be felt. The first and second sounds were well heard at all areas. There was a loud systolic murmur heard best at the third left interspace and transmitted into the axilla. No diastolic murmur was audible at this area. The apex of the heart was in the fifth interspace. Just inside the anterior axillary line, a systolic

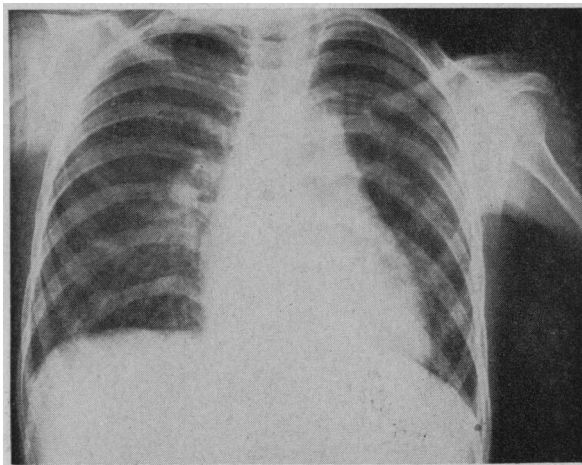


Figure 1.—In a roentgenogram of the chest an increase in the size of the heart shadow, and congestion and engorgement of the pulmonary vessels were noted.

murmur of an entirely different pitch was audible. This murmur was not transmitted.

The edge of the liver was palpated five fingers' breadth below the costal margin. It was moderately tender.

Definite evidence of right ventricular hypertrophy was noted in an electrocardiogram.

Under the fluoroscope the lung fields were observed to be clear in the periphery. The pulmonary arteries were prominent and pulsated fairly vigorously. The cardiac shadow was considerably enlarged, particularly in the region of the right ventricle. In the left oblique view a very good right ventricular shelf was observed, and it was noted that there was no enlargement of the left ventricle.

"In examination of the blood, slight polycythemia was noted. There was no leukocytosis. The erythrocyte sedimentation rate was 27 mm. in one hour."

The consultant's diagnosis was: (1) congenital heart disease; (2) interatrial septal defect; (3) right ventricular hypertrophy; (4) congestive heart failure confined entirely to right ventricular failure. He commented:

"The fact that the patient was poorly developed was the first consideration which led to the diagnosis of congenital heart disease. Pure right-sided heart failure without evidence of pulmonary disease is usually due to a congenital lesion involving the right side of the heart. The fact that the cyanosis did not come on until the second attack of heart failure was of significance. The systolic murmur and thrill, felt best in the third left interspace at the peristernal line, was strongly suggestive of overloading of the pulmonary circulation as a result of a shunt somewhere within the heart. The faint apical systolic murmur was probably secondary to moderate dilatation. It was possible to definitely rule out coarctation of the aorta, patent ductus arteriosus, transposition of the great vessels, and tetralogy of Fallot, since the lungs were well supplied with blood. A moderate degree of pulmonary stenosis, probably valvular, seemed probable." It was suggested that the patient be kept at rest, that large quantities of distilled water be given in order to prevent thrombosis, and that administration of digitalis be continued until all signs of heart failure had disappeared. The consultant suggested that a cardiac catheterization then be carried out because of the pulmonary stenosis, which he believed could be relieved. He felt that, with the stenosis relieved, the interatrial septal defect should not throw too great a strain on the right heart.

The child continued to be dyspneic, even while at complete rest. There was no edema noted in the genitalia or

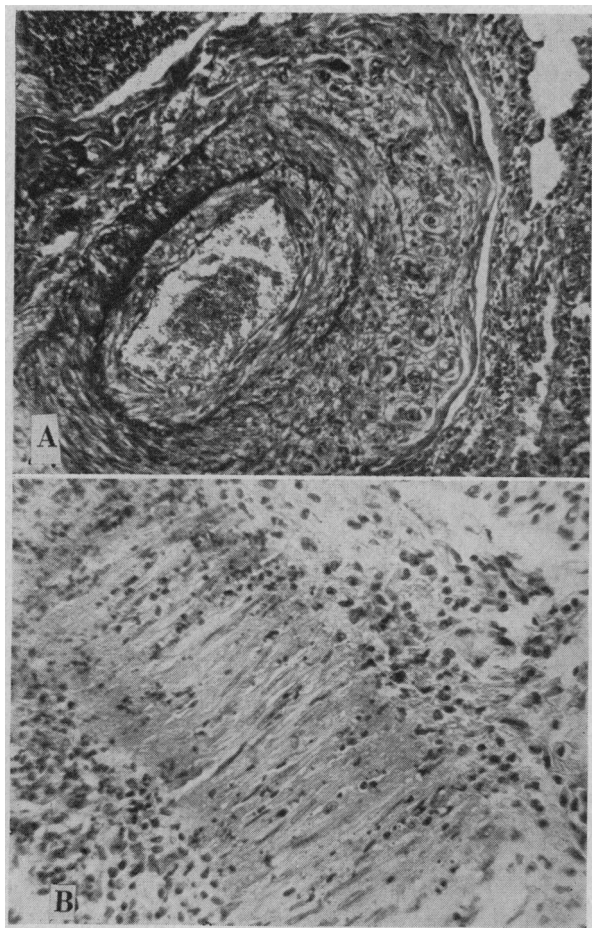


Figure 2.—A—A small muscular pulmonary artery. Note subendothelial proliferation, partial destruction of the wall and fragmentation of the elastic fibers. (Weigert's elastic stain). B—Higher magnification of the artery. The wall is infiltrated by lymphocytes. (Hematoxylin and eosin stain.)

sacral region or in the extremities. The condition of the patient became poor and she died September 14, 1950, four months after the onset of the acute symptoms.

#### AUTOPSY REPORT

The body, embalmed, was that of a slenderly built, poorly nourished 9-year-old Mexican female child, 44 inches (112 cm.) in length. There was no free fluid in the abdominal cavity. The lower edge of the liver extended 8 cm. below the xiphoid process. There was no clubbing of the finger tips or toes.

The right pleural cavity contained 500 cc. of a yellow fluid, and the left pleural cavity 400 cc. The pericardial sac was dilated and extended from the right costochondral junction to the left anterior axillary line. It contained about 25 cc. of clear fluid.

The heart weighed 170 grams (normal 110 grams). The large vessels were normal in location. The apex was made up by the right ventricle. The wall of the left ventricle averaged 8 mm. in thickness while the wall of the right ventricle was 10 mm. thick. The tricuspid valve was 85 mm. in circumference. There was pronounced dilation of the right auricle and the right ventricle. Circumference of the aorta was 37 mm., of the pulmonary artery 46 mm. There was an occasional fatty plaque in the intima. The mitral ostium was 42 mm. in circumference. The foramen ovale was closed;

there were no evidences of a ductus arteriosus. Both coronary ostia arose from the aorta. The right ostium of the coronary artery was slightly larger than the left. Occasional fatty plaques were noted in the intima of the aorta. The myocardium was moderately firm and deep brown.

The right lung weighed 150 grams. The upper lobe appeared smaller than the middle and lower lobes. All the lobes felt firm. The pleura was smooth and glistening. When sectioned the parenchyma of the lung was observed to be dark purple and slightly moist with blood. The bronchi were everywhere free. The branches of the pulmonary artery appeared dilated, and the intima contained an occasional fatty plaque. The lumen was free. The left lung weighed 140 grams. The edges were crepitant and there were no remarkable abnormalities noted.

The liver weighed 620 grams. It was firm and the surface smooth. The sectioned surface of the parenchyma was dark reddish-brown with distinct acinar markings. The spleen, which weighed 80 grams, was firm and the pulp on sectioned surface was deep purple-red and moist. The follicles were distinct.

About equal in size, the kidneys together weighed 130 grams. The capsules were stripped with ease, leaving a smooth purple-tan surface. The average diameter of the sectioned surface of the cortex was 6 mm. The markings were distinct.

The brain was not examined. No abnormalities were noted in other organs.

#### Microscopic Examination

**Heart:** The muscle fibres of the left ventricle appeared narrow and the nuclei were distinct. In the epicardium there were occasional foci of lymphocytes. No abnormality was noted in the branches of the coronary artery and vein. Muscle fibers of the right ventricle were about four times the diameter of those in the left ventricle and many of the nuclei were large. There was loose infiltration of large mononuclear and polymorphonuclear cells into the epicardium and for a short distance into the myocardium. No Aschoff nodules were observed.

**Pulmonary artery:** In sections taken from the main artery and also from its branches, pronounced thickening of the wall was noted. Many of the endothelial cells were swollen and the intima was thickened and infiltrated with lymphocytes and large mononuclear cells. There was an occasional focus of fibrinoid necrosis in the intima. In a few places in the adventitia infiltrations of lymphocytes were noted.

**Lungs:** In sections taken from numerous areas, collapsed alveoli and dilated capillaries engorged with red cells were observed. Many of the bronchi were dilated, many were occluded by mucous and desquamated epithelial cells, many were surrounded by polymorphonuclear leukocytes, plasma cells and lymphocytes. In examination of the branches of the pulmonary artery, obliteration of the lumen by an active fibroblastic tissue rich in young capillaries was noted in many places. Fibrinoid necrosis of the walls of some of these capillaries was noted; in many such instances only a narrow slit of lumen remained. There was thickening of the walls, particularly the intima and media, of many of the arterioles; the elastic tissue appeared increased and thickened, particularly the external limiting membranes. In some of the arterioles the lumen was completely obliterated by the subendothelial fibrous proliferation (Figure 3) while in other muscular arteries there was obliteration and recanalization of the lumen (Figure 4). Some of the arterioles contained thrombi. In some of the arterioles the endothelial cells were proliferated and swollen and appeared to be hydropic. Only rarely observed in the arterioles was a suggestion of nodular thickening of the wall. In some of the branches in which proliferation of cells, particularly lymphocytes and monocytes, was noted, polymorphonuclear leukocytes were inconspicuous.

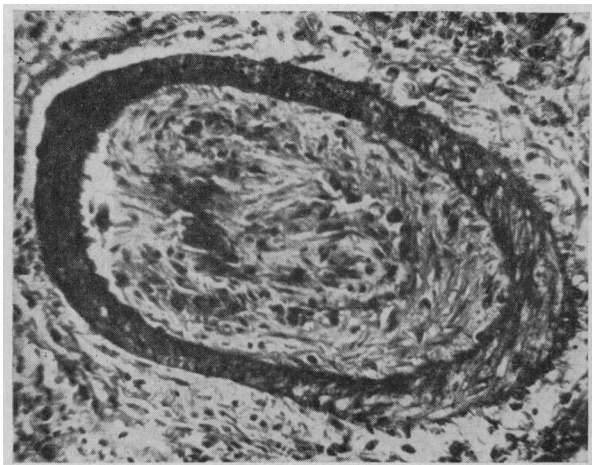


Figure 3.—Subendothelial fibrous proliferation completely obliterating the lumen of a small muscular pulmonary artery. (Weigert's elastic stain.)

One vessel was infiltrated with polymorphonuclear cells and lymphocytes rather typical of periarteritis nodosa. In some of the vessels the changes were much like those observed in the healing stage of periarteritis nodosa.

#### DISCUSSION

In the case here reported, the lesions were restricted to the pulmonary arterioles. A variety of pathologic changes were noted. Pronounced endothelial proliferation was noted in the earliest lesion. Many of the cells were ballooned with a vacuolated cytoplasm. These changes were followed by subendothelial fibrous proliferation. In some of the arterioles there was lymphocytic infiltration throughout the media and adventitia, while the majority of the smaller vessels were thickened, chiefly by subendothelial fibrosis, to such an extent that the lumen was narrowed or completely obliterated. Recanalization of the lumen was noted in some of the obliterated arterioles.

The media of the main pulmonary artery appeared to be vacuolated and there were cystic areas. In the main branches, focal thickening of the intima was frequently noted.

The sclerosis of the pulmonary arteries and the pulmonary arterioles was responsible for the pronounced pulmonary hypertension which in turn caused the hypertrophy of the right ventricle.

The short duration of the symptoms and the periodic fever would suggest an infectious process such as that of rheumatic fever, but in the postmortem examination of the heart nothing to support a diagnosis of rheumatic fever was noted. Although thrombi and nodular thickening typical of the healed stages of periarteritis nodosa were noted, these changes were not conspicuous.

#### SUMMARY

A case in which a nine-year-old Mexican female had pathologic changes restricted to the pulmonary arteries is

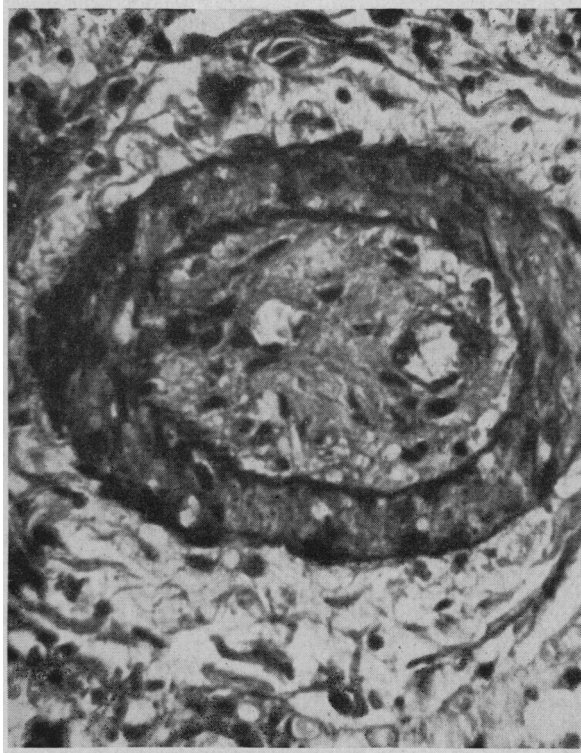


Figure 4.—A small muscular pulmonary artery with obliteration and recanalization of the lumen due to subendothelial fibrous proliferation. (Weigert's stain.)

reported. Pronounced cor pulmonale suggested long-standing pulmonary hypertension. The main changes confined to the arterioles consisted of endothelial proliferation, focal fibrinoid necrosis of the intima, arteritis, subendothelial fibrosis with narrowing and occlusion of the lumen, and recanalization of the obliterated lumen.

Clinical observations suggested congenital heart disease, interatrial septal defect and right ventricular heart failure.

The short duration of the illness suggested an infectious process. However, many of the changes in the arterioles were degenerative in nature and simulated those of arteriosclerosis.

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